REMARKS

Claims 12 and 16-29 are pending. Applicants have amended claims 16, 17 and 23 to clarify and further define the scope of the invention. Applicants have also added new claim 29.

Claims 12 and 18 have been amended to claim N-acyl derivatives of tryptophanyl-esters. Claims 16-17 and 19 -20 have been amended to reflect the amendment of claims 12 and 18.

Claims 12 and 18 have also been amended to recite that R_1 is a saturated C_1-C_{18} hydrocarbon residue. Support for this amendment may be found in the fact that the specification provides numerous examples of N-acetyl derivatives of tryptophanyl-esters. One having ordinary skill in the art would recognize that N-acetyl derivatives are when R_1 = 1.

Claims 12 and 18 have been further amended to improve their form by substituting the art-recognized term "hydrocarbon residue" for "carbon hydrogen residue." Support for this amendment may be found throughout the specification. See, e.g., originally filed claim 2, which recites a number of residues that one having ordinary skill in the art would recognize as hydrocarbons of the tryptophanyl-esters or their N-acyl derivatives.

Claims 12 and 18 also have been amended to correct the structure of the claimed compound. Support for this amendment may be found on page 6, line 5.

Claims 16 and 17 have been amended to exclude N-oleoyl-tryptophanethyl-ester. Support for this amendment appears in claim 12 which specifies that "R_1" in the formula is a saturated C_1-C_{18} carbon hydrogen residue.

Claims 17 and 20 have been amended to clarify that the N-acetyl derivative is an N-acyl derivative. One having ordinary skill in the art would recognize that an N-acetyl derivative is a subset of an N-acyl derivative, wherein R_1 = 1.

Applicants have amended claim 23 to correct a typographical error. Applicants have replaced the term "immunosuppressiva" with "immunosuppressive."

Applicants address the Examiner's objection below:

<u>35 U.S.C. § 112, 2nd paragraph: Claims 16-17, 19, 20 and 23</u>

The Examiner has rejected claims 16-17, 19, 20 and 23 under 35 U.S.C. § 112, second paragraph as being indefinite. Specifically, the Examiner contends that there is insufficient antecedent basis for the limitation "N-acetyl-" in claims 16, 17, 19 and 20. Furthermore, the

Examiner asserts that the term "immunosuppressiva" in claim 23 is indefinite.

Applicants respectfully submit that as amended, claims 16, 17, 19 and 20 are definite.

Amended claim 12 recites any N-acyl derivatives of tryptophanyl-esters in which R_1 is a saturated C_1-C_{18} hydrocarbon. The limitation "N-acetyl-" recited in dependent claims 16, 17, 19 and 20 refer to compounds with the formulation: N-C(O)CH_3, which is covered in the case in which R_1 = 1. Thus, the limitation "N-acetyl" recited in claims 16, 17, 19 and 20 are clearly supported by claims 12 and 18, from which they depend.**

Applicants have also amended claim 23 to replace the term "immunosuppressiva" with the term "immunosuppressive," thus obviating the Examiner's rejection.

35 U.S.C. § 103

Claims 12 and 16-17: Kathawala

The Examiner has rejected claims 12 and 16-17 under 35 U.S.C. § 103 as being obvious over U.S. Patent

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** Applicants submit that the Examiner's reference to the limitation "N-acetyl-tryptophanethyl-ester" in claims 19 and 20 is incorrect because it is not recited in the claims.

4,448,785 ("Kathawala"). According to the Examiner, Kathawala teaches N-acyl tryptophan compounds including N-oleoyl-tryptophanethyl-ester (when R_1 is ethyl, R_2 and R_3 are hydrogens, A is oleyl) which are useful as anti-cholesteric agents. Furthermore, the Examiner asserts that Kathawala teaches that the N-acyl tryptophan compounds may be formulated into solid or liquid pharmaceutical compositions such that it would have been obvious to one of skill in the art at the time the invention was made to employ N-oleoyl-tryptophanethyl-ester specifically in a pharmaceutical composition. Applicants respectfully traverse.

Kathawala discloses various unsaturated fatty acid amides of tryptophan derivatives which are useful as anti-atherosclerotic agents. In contrast, amended claim 12 recites a pharmaceutical composition comprising an N-acyl derivative of a D- or L-tryptophanyl-ester wherein the X is $C(O)R_1$ and R_1 is a saturated C_1-C_{18} carbon hydrogen residue. Kathawala does not disclose, teach or suggest N-acyl derivatives of tryptophan comprising saturated fatty acid amides as recited in amended claim 12.

Thus, Kathawala does not render the claimed invention obvious.

Claims 18-19 and 21-28: Nakamiya in view of Stites

The Examiner has rejected claims 18-19 and 21-28 under 35 U.S.C. § 103 as being obvious over Nakamiya et al., Hakko Kogaku Zasshi, 54(6):369-373 (1976) ("Nakamiya") in view of Stites et al., Basic & Clinical Immunology, 5th Ed., 184:34, 36-37 (1984) ("Stites"). Specifically, the Examiner asserts that Nakamiya teaches that lauryl esters of different amino acids including tryptophan having anti-bacterial activities. The Examiner states that Nakamiya does not teach that lauryl esters of tryptophan are useful, alone or in combination, with another active agent for formulating a pharmaceutical composition. Further, the Examiner admits that Nakamiya does not expressly teach that stearyl or palmityl esters of tryptophan are useful for the same purpose. However, the Examiner asserts that Stites teaches that immunoglobulin M has a high antibacterial activity such that it would have been obvious for one of ordinary skill in the art at the time the invention was made to employ the lauryl ester of tryptophan, alone or in combination with immunoglobulin M, for formulating a pharmaceutical composition. The Examiner states that combining two agents known to be useful for the same purpose is *prima facie* obvious.

Similarly, the Examiner contends that it would have been obvious to one of skill in the art at the time the invention was made to employ stearyl or palmityl esters of tryptophan, alone or in combination, with immunoglobulin M for formulating a pharmaceutical composition with a reasonable motivation and expectation of success because lauryl and stearyl or palmityl esters are similar esters with similar properties. Applicants respectfully traverse.

Nakamiya purports to disclose the lauryl ester of DL-tryptophan. However, Nakamiya does not disclose, teach or suggest N-acyl derivatives of D- or L-tryptophanyl-esters, nor provides any motivation for making these compounds. Stites, which is cited for teaching that immunoglobulin M has a high antibacterial activity, does not remedy this deficiency. Thus, neither Nakamiya nor Stites, either alone or together, renders the claimed invention obvious.

CONCLUSION

Applicants request that the Examiner enter the amendments, consider the foregoing remarks and allow the pending claims.

Respectfully submitted,

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